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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Henry N Wixon
Hale & Dorr
Suite 1000
1455 Pennsylvania Avenue NW
Washington, DC 20004

EXAMINER	
GABEL, GAILENE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 06/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,170	ERIC ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☒ Claim(s) *8-14 and 17* is/are objected to.

8)☒ Claim(s) *1-18* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.0-0

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group 1, claims 1-17, with traverse, is acknowledged and has been entered. Claim 18 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on March 22, 2005. Currently, claims 1-18 are pending. Claims 1-17 are under examination.

2. Applicant argues that Groups I and II are so closely linked and drawn to the same inventive concept, namely the use of intracellular immunoglobulins; hence search and examination of both groups together would not pose serious burden on the Examiner.

Contrary to Applicant's argument, Group II is drawn to method of preparing intracellular immunoglobulins as opposed to Group I which is drawn to use of intracellular immunoglobulins; hence, Groups I and II are rendered independent and distinct as they have separate structural requirements which require separate fields of search, i.e. generating immunoglobulins versus using selected immunoglobulins in a functional assay. Literature search for each method is distinct since the structural requirements of each invention are different. While searches would be expected to overlap, there is no reason to expect the searches to be coextensive. Because these

inventions are distinct for the reasons given above and have acquired a separate status in the art, restriction for examination purposes as indicated is proper.

Oath/Declaration

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because it does not identify the citizenship of one of the inventors. In this case, the citizenship of Michela Visentin is missing.

Information Disclosure Statement

4. The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609 subsection III. A(1) states, "the list ... must be submitted on a separate

paper." Therefore, the references cited in the Search Report have not been considered. Applicant is advised that the date of submission of any item of information or any missing elements will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609 subsection III. C(1).

Priority

5. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(a)-(d) based upon an application filed in United Kingdom, 9905510.5, on March 10, 1999.

Claim Objections

6. Claims 8-14 and 17 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim in reciting, "A method according to any preceding claim." Claims 8, 10, 11, and 17 are specifically in improper dependent form. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, preamble is indefinite in failing to recite a positive limitation in reciting, "determining the ability of an immunoglobulin to bind a target". Perhaps, Applicant intends, "determining binding of an immunoglobulin to a target".

Claim 1, step b) is confusing and lacks clear antecedent basis in reciting, "an intracellular immunoglobulin" because it is unclear as to whether the "intracellular immunoglobulin" is intended to be the same element in the claim as the "immunoglobulin ... in an intracellular environment" recited in the preamble.

Claim 1, step b) is ambiguous because it is unclear what Applicant intends to encompass in reciting, "providing an intracellular immunoglobulin which is associated with the first molecule" because it is unclear what Applicant intends to encompass in reciting, "providing" as used in the claim, i.e. how the intracellular immunoglobulin is "provided" for [operative] association with the first molecule. Further, claim 1, step b) appears to imply but fails to specifically define that the first molecule is an intracellular molecule within the intracellular environment.

Claim 1, step c) is ambiguous because it is unclear what Applicant intends to encompass in reciting, "providing an intracellular target which is associated with the second molecule" because it is unclear what Applicant intends to encompass in reciting, "providing" as used in the claim, i.e. how the intracellular target is "provided" for [operative] association with the second molecule. Further, claim 1, step c) appears to

imply but fails to specifically define that the second molecule is an intracellular molecule within the intracellular environment.

Claim 1, step c) is vague and indefinite in reciting, "such as the association of the immunoglobulin with the target leads to stable interaction of the first and second molecules" because the term "associated" is a subjective term that lacks a comparative basis for defining its metes and bounds. Such recitation does not appear to be supported by Applicant's disclosure of the term, "operative association" in page 7, lines 23-29. Based on the preamble, it appears that Applicant intends the term "binding". Additionally, it is unclear as to whether the stable interaction in step c) intends to be distinct, i.e. a change, from the stable interaction between the first molecule and the second molecule in step a), since step c) lacks clear antecedent basis in reciting, "stable interaction". Perhaps, Applicant intends, "such as the binding of the immunoglobulin with the target leads to the stable interaction of the first and second molecules.

Claim 1, step d) lacks clear antecedent support in reciting, "the intracellular interaction". Perhaps, Applicant intends, "assessing intracellular binding between... and the stable interaction between first molecule and the second molecule".

Claims 2-17 have improper antecedent basis problems in reciting, "A method according to ...".

Claim 3 lacks clear antecedent basis in reciting, "first and second molecule associate to form" because claim 1 recites that they are in "stable interaction".

Claim 15 is indefinite in reciting, "comprising further the step of e) isolating those immunoglobulins which give rise to a signal" because it is how this method step relates to the method recited in claim 1 which is a method for determining binding between immunoglobulin and target in an intracellular environment.

Claim 16 is indefinite in reciting, "comprising further the step of f) subjecting the selected immunoglobulins to a functional intracellular assay" because it is how this method step relates to the method recited in claim 1 which is a method for determining binding between immunoglobulin and target in an intracellular environment.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Gargano et al. (From Phage Libraries to Intracellular Immunization, Intracellular Antibodies: Development and Applications (1997) Chapter 10, pages 174-186)).

Gargano et al. teach determining efficient binding between intracellular immunoglobulins (scFv) expressed in a yeast two hybrid format and corresponding target antigens in an intracellular environment (yeast cells), and isolating immunoglobulins which bind successfully (see page 176, second full paragraph, and Figure 10.1). Gargano et al. provide an interaction trap (two hybrid system) having a

first molecule and a second molecule in a modular domain structure as in eukaryotic transcription factors: transcriptional activation domain and a DNA-binding domain, which exist as separable domains, but associate to form an active reporter molecule (construct). Activation of the reporter construct occurs when the two domains, expressed as activation domain (VP16) and DNA-binding domain (LexA) fusion proteins, are brought together through binding interaction of two polypeptides that are associated (fused) thereto in an assay, leading to generation of a signal that can be monitored by change in optical property (colorimetric assay). The two polypeptides are an scFv fragment and a target antigen associated (fused) to each of the VP16 activation domain and LexA DNA-binding domain, respectively. According to Gargano et al., the level of reporter activation correlates well with specific binding of proteins which further gives an indication of the strength of the interaction (see page 174, fourth full paragraph to page 176, first full paragraph). The active reporter molecule may be an enzyme and the method is performed in the presence of a substrate (see page 177, first full paragraph and Figure 10.1 (D)). The immunoglobulins are provided by immunoglobulin-encoding nucleic acids within mammalian cells, from phage libraries encoding a repertoire of immunoglobulins (see page 177, second to fourth full paragraphs). The libraries can be constructed from nucleic acids isolated from an organism which has been challenged by antigen (see page 180, first and second full paragraph). Gargano et al. teach selecting immunoglobulins and further subjecting them to functional intracellular assay (see Figure 10.2). Cells can be sorted (rescued) on the basis of phenotype conferred by the intracellular immunoglobulins.

9. No claims are allowed.

Remarks

10. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Fields et al. (US Patent 5,468,614) disclose a method and kit for detecting interaction between two proteins wherein a first hybrid containing DNA binding domain of a transcriptional activator is fused to the first protein and a second hybrid contains a transcriptional activation domain fused to the second protein, and when the two proteins interact, they bring into close proximity the two domains of the transcriptional activator, sufficient to cause transcription, which can be detected by the activity of the marker gene which contains a binding site for the DNA-binding domain. See Summary.

Nandabalan et al. (US Patent 6,057,101) disclose a method for detecting interaction between two populations of proteins wherein the proteins are fused to DNA-binding domain of a transcriptional activator or to the transcriptional activation domain of the transcriptional activator. Productive interaction between the two halves due to protein-protein interactions lead to the reconstitution of the transcriptional activator, which in turn leads to the activation of a reporter gene containing a binding site for the DNA binding protein. See Summary.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
June 6, 2005